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Prophylactic Intra-Arterial Injection of Lidocaine Prevents Trigemino-cardiac Reflex During Endovascular Embolization for Dural Arteriovenous Fistula: A Report of 2 Cases

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

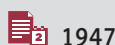
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Conflict of interest: None declared

Case series**Patients:** Male, 56-year-old • Male, 57-year-old**Final Diagnosis:** Trigemino-cardiac reflex**Symptoms:** Bradycardia • severe hemodynamic fluctuation**Medication:** —**Clinical Procedure:** —**Specialty:** Anesthesiology • Neurosurgery**Objective:** Unusual clinical course**Background:** Trigemino-cardiac reflex (TCR) is a unique brain stem reflex that manifests as the sudden onset of hemodynamic perturbation in heart rate and blood pressure as a result of stimulation of any branches of the trigeminal nerve. Onyx™ embolization in cerebrovascular interventional surgery can trigger TCR, leading to severe hemodynamic fluctuations and even cardiac arrest. Appropriate prophylactic approaches to prevent Onyx™ embolization-induced TCR are still lacking.**Case Reports:** We report the cases of 2 patients with recurrent and profound bradycardia due to TCR during endovascular Onyx™ embolization for a dural arteriovenous fistula. Prophylactic intra-arterial injection of lidocaine (10-20 mg) effectively and safely blocked the recurrence and potential occurrence of TCR. These 2 patients had reduced heart rate with either hypotension or hypertension during their TCR episodes, suggesting that stimulating a distinct cerebral artery (occipital artery versus vertebral artery branch) can initiate TCR by provoking the vagus nerve via the common neuronal pathway while simultaneously inhibiting or exciting the sympathetic pathway.**Conclusions:** Intra-arterial injection of lidocaine during endovascular procedures can be recommended as an effective prophylactic approach for use in the treatment of the cerebrovascular disorder where there is high risk of embolization-induced TCR.**Keywords:** Embolization, Therapeutic • Injections, Intra-Arterial • Lidocaine • Reflex, Trigemino-cardiacFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/930837>

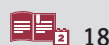
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Background

Trigemino-cardiac reflex (TCR) is an experimentally and clinically well-established brainstem reflex that manifests as the sudden onset of hemodynamic perturbation, defined as a drop of heart rate and mean arterial blood pressure of at least 20% from the baseline upon the stimulation at any branches of the trigeminal nerve [1]. TCR occurs in skull base surgery, ophthalmic and dental surgery, trigeminal rhizolysis, and any other procedures related to the stimulation of the trigeminal nerve [2]. TCR generally occurs during endovascular embolization in the treatment of cerebrovascular disorders involving intradural or dural pathology, especially dural arteriovenous fistula (DAVF) [3]. Recently, Onyx™ endovascular embolization therapy has been widely used for the treatment of DAVF [4].

Most of the TCR episodes are transient. However, there are increasing concerns about the TCR generated by Onyx™ embolization in cerebrovascular interventional surgery as it can lead to irreversible cerebrovascular accidents, neurological damage, and even cause severe hemodynamic fluctuations and cardiac arrest [5]. It is hard to predict the occurrence of TCR during endovascular embolization in the treatment of the cerebrovascular disorder, and appropriate prophylactic approaches to prevent embolization-induced TCR are still lacking. Here, we report 2 cases in which a TCR episode occurred during Onyx™ endovascular embolization in DAVF, which was effectively and safely blocked by prophylactic intra-arterial injection of lidocaine.

Case Reports

Case 1

A 56-year-old man presented to the Neurosurgical Emergency Department with sudden dizziness, convulsion, and loss of consciousness. A computed tomography (CT) scan showed multiple small hematomas in the right occipital parietal lobe, and the symptoms improved after 2 weeks of symptomatic treatment. Subsequent digital subtraction angiography (DSA) suggested a right cavernous sinus DAVF (Borden type I) with artery constituent of the right middle meningeal artery and the branch of the occipital artery (**Figure 1A**).

The patient was previously healthy, with no history of hypertension or heart disease, and required intravascular interventional embolization under general anesthesia. Anesthesia was induced with no hemodynamic abnormalities and maintained by inhalational-intravenous anesthesia. The right femoral artery was punctured, a 6 Fr Envoy guide catheter (Cordis Endovascular, USA) was positioned in the proximal occipital artery, and angiography was performed. An Echelon 10 microcatheter (EV3, USA) was advanced over a Transcend

microglidewire (EV3, USA) into the meningeal branch of the occipital artery of the DAVF.

When the microcatheter was in a stable position, embolization of the fistula was performed. With a few dimethyl sulfoxide (DMSO) injections, the patient experienced bradycardia (the heart rate decreased quickly from 61 bpm/min to 43 bpm/min), followed by a drop of blood pressure from 113/59 mmHg to 96/49 mmHg. The injection was immediately paused and normal sinus rhythm returned spontaneously and quickly. The patient was then considered to have TCR. After the patient was stabilized, 10 mg lidocaine was injected into the local arterial and there is no hemodynamic response observed. After 2 min, a second DMSO injection was performed and there were no more cardiac episodes during the subsequent procedure.

Further angiography revealed that the middle meningeal artery was also involved in the DAVF, so embolization was continued. In view of the risk of TCR and the potential effect of lidocaine, after the catheter was in a stable position, 20 mg lidocaine was injected into the artery fistula. DMSO and Onyx™ were subsequently serially injected without any abnormal hemodynamic response. Proper angiographic occlusion of the fistula was achieved and final angiography showed no thromboembolic complications as a result of the procedure (**Figure 1B**).

The patient was extubated without any additional neurological symptoms, and was transported to the Neurocritical Care Unit for recovery. There was no postoperative hemodynamic instability and the patient was discharged on the third day.

Case 2

A 57-year-old man was admitted with ongoing dizziness and headaches. Magnetic resonance imaging (MRI) showed multiple cerebrovascular stenosis and a DAVF (Borden type I) with bilateral vertebral artery branches involved. The patient was otherwise well, with no significant cardiac history and ECG results were normal. He elected to proceed with endovascular treatment of the fistula under general anesthesia.

Considering the high risk of TCR in embolization of the vertebral artery branch and the success of prophylactic lidocaine to prevent TCR in case 1, we recommended that the neurosurgeons administer a local intravascular injection of lidocaine before embolization. He was injected with 10 mg lidocaine into the right vertebral artery branch (**Figure 2A**). The hemodynamics were stable and no TCR was observed during the entire embolization (**Figure 2B**). To confirm the specificity of the effect of lidocaine on TCR, lidocaine was not injected before left vertebral artery branch embolization (**Figure 2C**). During injection of 0.5 ml DMSO, the patient had a TCR episode in which the heart rate quickly dropped from 68 bpm/min to 46 bpm/min,

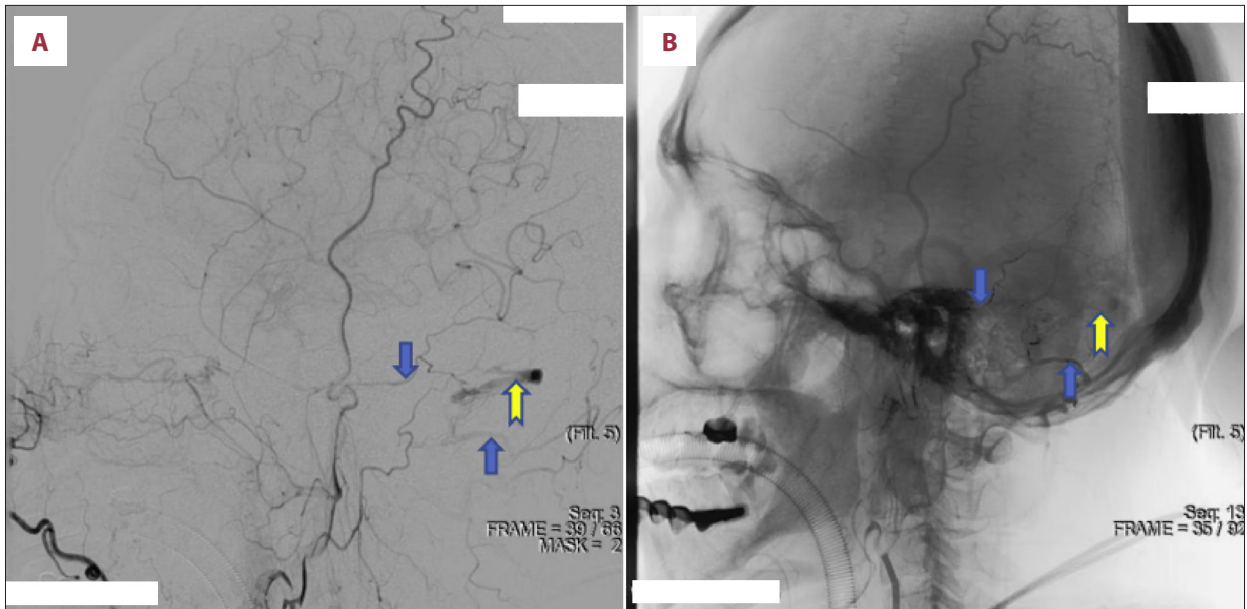


Figure 1. (A, B) The DSA images in case 1. The yellow arrows indicate the DAVF site, and the blue arrows indicate the feeding artery. The DAVF was supplied by the branches of the middle meningeal artery and occipital artery.

and, as unexpected, was followed by increased blood pressure from 122/73 mmHg to 155/84 mmHg. The injection was immediately paused, and the heart rate and blood pressure gradually returned to normal levels within 2 min. Subsequently, 10 mg lidocaine was injected intra-arterially, and there was no similar fashion occurred during DMSO reinjection and the following embolization procedure (Figure 2D).

The patient awoke well, but muscle strength of the left limb was decreased slightly compared with that before surgery; the condition was considered to be related to multiple cerebrovascular stenoses before surgery and the perioperative vasospasm. After 3 days of vasodilator therapy, the patient's muscle strength of the left limb was mostly restored without obvious sequelae, and he was discharged on the fifth day.

Discussion

We report 2 cases of TCR during endovascular Onyx™ embolization for DAVF. During the operations, the circulation was stable before DMSO injection. Upon the endovascular injection of DMSO, the heart rate immediately decreased by >20%, a distinguishing feature of TCR episodes. These 2 cases both presented a sudden decreased heart rate by >20% and the normal sinus rhythm quickly returned when DMSO injections were stopped. However, blood pressure changed slightly in both cases, which is not typical for TCR. We always closely monitored the patient's vital signs during endovascular embolization for dural arteriovenous fistula to avoid potential TCR-induced severe hemodynamic fluctuations and even cardiac

arrest. Therefore, once the decreased heart rate occurred following endovascular embolization, we always immediately tell the neurosurgeons and let them stop the injection promptly. This might be the reason why there was less alteration of blood pressure following a decreased heart rate and then lack of the typical presentation of TCR in these 2 patients.

In both cases, there were 2 artery vessels linking to each lesion site. DMSO injection into one of these 2 vessels caused TCR, and 10-20 mg lidocaine injection prevented TCR recurrence. Consistently, serving as a self-control test, prophylactic injection of lidocaine into the other vessel did not cause TCR. Therefore, local intravascular injection of a small dose of lidocaine can effectively inhibit TCR caused by cerebrovascular embolization. We found that 10-20 mg lidocaine injection into the cerebral artery effectively inhibited TCR incidence without adverse effects on the central nervous system, demonstrating that the prophylactic application of low-dose lidocaine is safe and effective. Our present results are consistent with a recently published case report [6] that 5 mg lidocaine could prevent TCR during endovascular treatment of a carotid-cavernous fistula.

The physiological mechanism of TCR is that signals triggered by either peripheral or central stimulation are sent to the sensory nucleus of the trigeminal nerve, and then along the short internuncial nerve fibers in the reticular formation, relayed to the efferent pathway in the motor nucleus of the vagus nerve and nucleus ambiguus. The fibers of the vagus or sympathetic nerves end in the myocardium, leading to autonomic changes that usually manifest as a negative chronotropy [7]. The

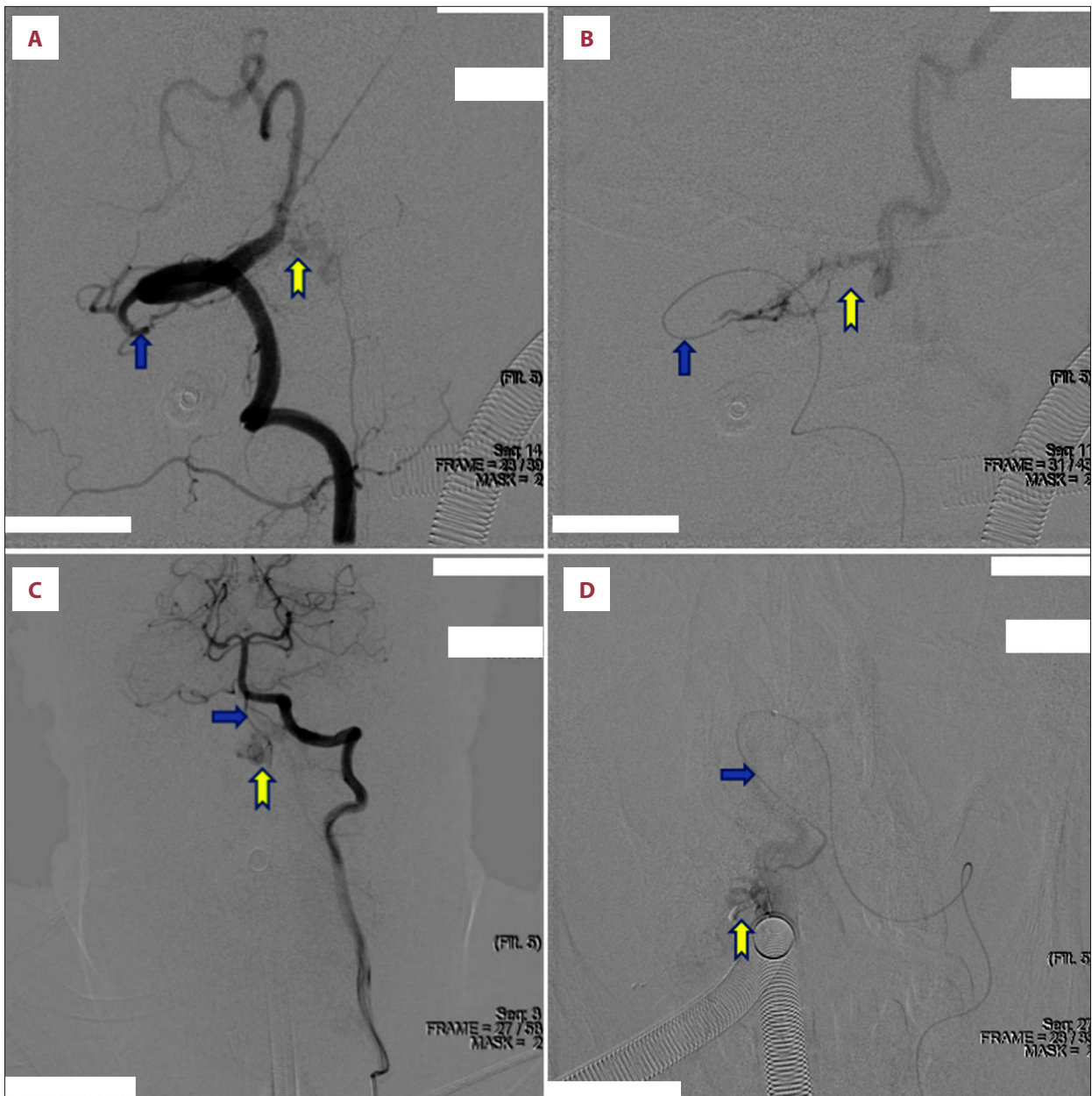


Figure 2. The DSA images in case 2. The DAVF was supplied by bilateral vertebral artery branches: the right (A, B) and left one (C, D). A and C were pre-embolization, but B and D were post-embolization. The yellow arrows indicate the DAVF site, and the blue arrows indicate the feeding artery.

dura mater is innervated in part by branches of the trigeminal nerve and receives vascular supply from the meningeal artery and meningeal branches of the occipital artery [8]. These vessels are mostly involved in the blood supply to the sensory area of the trigeminal nerve. Hence, embolization with Onyx™ or DMSO inside these vessels can mechanically or chemically stimulate the trigeminal nerve and cause a TCR.

There are 2 major subtypes of peripheral or central TCR. Peripheral stimulation of the trigeminal nerve co-activates vagal

and sympathetic nerves, resulting in both hypertension (peripheral vasoconstriction) and bradycardia [9]. By contrast, central stimulation causes hypotension and bradycardia by generating profound activation of the cardiac vagal branch and distinct inhibition of the inferior cardiac sympathetic nerve [10]. In this report, we observed 2 patients who presented reduced heart rate accompanied by either hypotension (case 1) or hypertension (case 2), suggesting that central stimulation from chemical agents at distinct cerebrovascular embolization sites might share a common efferent pathway for vagus activation,

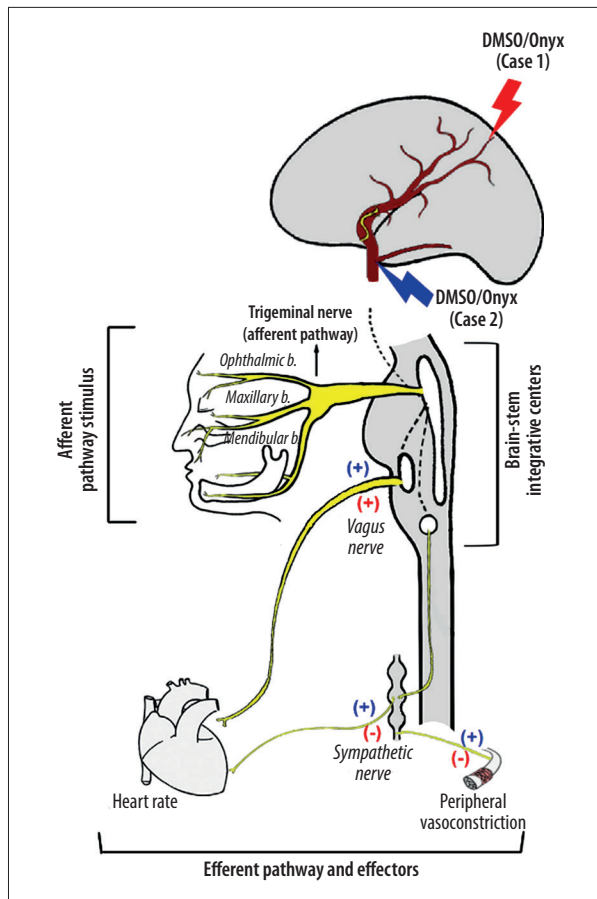


Figure 3. Schematic illustration of the autonomic neural pathways and effectors activated as a consequence of trigeminal nerve stimulation triggered either by peripheral signals from ophthalmic, maxillary, and mandibular branches or central cerebral vascular stimulus (figure modified from Buchholz's publication [18]). The central TCR, which was stimulated by DMSO/Onyx injection in the central vessel, induces a strong depressive response by a reciprocal activation of the parasympathetic system and an inhibition of the sympathetic system (red symbols). The peripheral TCR, which was stimulated by DMSO/Onyx injection in the peripheral vessels, involves simultaneous co-activation of both autonomic limbs (blue symbols).

but inhibit or promote the effect on the efferent sympathetic pathway (Figure 3).

In these 2 cases, the surgical procedures stimulated extratrigeminal nerve anastomosis, resulting in the decreased heart rate as the first sign of hemodynamic parameter change. According to the new TCR classification [11], the extratrigemino-cardiac reflex is classified as type IV reflex, while the TCR with the heart rate being the first changing parameter is labeled as class A reflex. Therefore, the 2 TCR reflex in the present report could be classified as type IVA reflex.

Currently, preventive measures for TCR mainly include the use of anticholinergic drugs and local nerve blocks [12]. However, there is concern that preemptive administration of anticholinergics for the prevention of TCR may be ineffective [13]. Bradycardia and hypotension in TCR could result from both excessive vagal activation and inhibition of adrenergic vaso-constriction, as observed after electrical stimulation of the spinal trigeminal tract and trigeminal nuclear complex [14]. Atropine can only block the cholinergic fibers, and cannot completely prevent bradycardia or hypotension. In addition, atropine carries a risk of refractory arrhythmia, so prophylactic use is not recommended [15]. Local anesthetic infiltration or block of the nerve(s) involved in the afferent neuronal pathway may accomplish a prophylaxis of the peripheral TCR. Nevertheless, nerve block is complex and may increase the risk of intracranial hemorrhage and infection during cerebrovascular interventional surgery. Intraoperative application of topical lidocaine is successfully used to prevent TCR recurrence in trigeminal nerve microvascular decompression [16]. However, topical anesthesia is not applicable for the TCR caused by mechanical stimulation of the trigeminal nerve during Onyx™ embolization since it is an interventional vascular procedure rather than open surgery.

Based on the knowledge that local intravenous injection of lidocaine can effectively prevent injection pain, we extrapolated it to the intra-arterial injection for cerebrovascular embolization surgery and expect to block both trigeminal nerve-activation and nerve-vascular communication. Indeed, lidocaine, as a prevailing voltage-gated sodium channel blocker [17], is capable of inhibiting the generation of action potential on the trigeminal nerve by acting on the afferent sensory nerve ending attached to the local vascular vessels and endothelial cells, thus acting as an endovascular anesthesia. Furthermore, lidocaine easily passes the blood-brain barrier; local injection of lidocaine might infuse into the perivascular tissues to block the trigeminal nerve branch, producing the effect of regional anesthesia.

Conclusions

Injection of 10-20 mg of intra-arterial lidocaine through an indwelling catheter not only blocked the recurrence of TCR, but also prophylactically prevented the potential occurrence of TCR, with no adverse effects in these 2 cases. Injection of intra-arterial lidocaine during endovascular procedures could be recommended as an effective prophylactic approach for use in the treatment of the cerebrovascular disorder where the embolization-induced TCR is too high-risk. To prove intra-arterial lidocaine injection feasible in the treatment of TCR, a large cohort study is unquestionably required to further explore the safety and effectiveness of this technique. Moreover, further detailed classification of subtype of central TCR might help neurosurgeons to predict its onset and severity and to use proper prophylactic approaches, including intra-arterial lidocaine administration.

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